



DEPARTMENT OF MEDICINE  
SCHOOL OF MEDICINE

March 11, 1999

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VETERANS ADMINISTRATION HOSPITAL  
3350 LA JOLLA VILLAGE DRIVE  
LA JOLLA, CALIFORNIA 92161

Dockets Management Branch  
U.S. Food and Drug Administration  
Department of Health and Human Resources  
Room 1061, HFA-305  
5630 Fishers Lane  
Rockville, Maryland 20852

**Docket Number 98P-0622**

To Whom It May Concern:

I am responding to the petition filed by Public Citizen Health Research Group to remove Rezulin (Troglitazone) from the market. As a specialist in the management of diabetes mellitus and its complications and a primary care provider for many patients with type 2 diabetes, I believe that such a decision by the FDA would be a major mistake. Although I am a speaker and consultant for many pharmaceutical companies, including Parke-Davis, who are involved with marketing medications for the treatment of diabetes, I am expressing my concern solely because of the effect such an action would have on the type 2 diabetic population.

Contrary to the statements made in the petition, I strongly believe many patients will suffer and ultimately develop complications and possibly die if this drug is removed from the market. It seems clear to me that while use of Rezulin can be associated with a rare severe idiosyncratic hepatocellular toxicity, this compound has truly transformed the lives of many type 2 diabetics by improving glycemic and metabolic control to a degree not achievable with other available medications.

This rare hepatotoxicity from Rezulin is even further reduced when liver function tests (ALT, AST) are monitored according to the current recommendations. The adverse effects, both in terms of morbidity and mortality, of inadequate treatment of type 2 diabetes is far greater than the toxicity of this compound and results in a risk-to-benefit ratio that I believe strongly favors continued availability of Rezulin.

In my clinical experience, there are many circumstances when addition of troglitazone to a failing diabetic treatment regimen has led to dramatic improvement in metabolic control. The additional benefits of this compound, on the classic diabetic dyslipidemia of high triglycerides, low HDL cholesterol and increased concentrations of small, dense, LDL particles is truly unique. This effect, combined with early, but provocative, evidence of potential cardiovascular benefits, is further compelling grounds to retain this compound in the therapeutic armamentaria of type 2 diabetes.

98P-0622

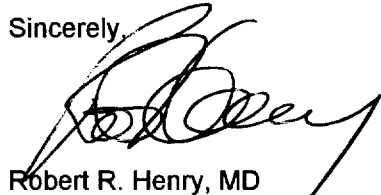
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Finally, I take issue with the petition statement that actual cases of hepatotoxicity are probably underreported. I believe this to be unlikely, and suspect rather, that adverse hepatic events may be over-reported in view of the extensive recent press and television publicity. Furthermore, many of the reported cases of hepatotoxicity may be guilt by association, rather than causal in nature.

The petition filed by Public Citizen Health Research Group has been a disservice to many patients with type 2 diabetes who, out of fear from the exaggerated publicity, have discontinued this medication unnecessarily and have had deterioration in metabolic control.

The availability of Rezulin has improved the lives of many patients with type 2 diabetes. It would be a regressive step to withdraw this medication and I trust that the committee and the FDA will see fit to deny the petition.


Sincerely,



Robert R. Henry, MD  
Professor of Medicine, UCSD  
Chief, Section of Endocrinology, Diabetes, & Metabolism  
VA San Diego Healthcare System

RRH/srw

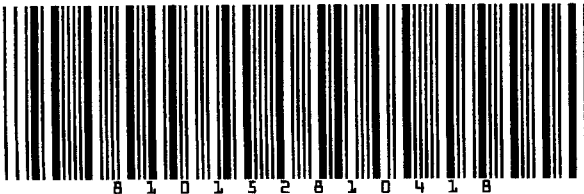
Cc: Kathleen Reedy, RDH, MS  
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**1 From**   
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**2 Your Internal Billing Reference Information**

**3 To**  
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